

State of the Art Review

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Regional Differences in the Epidemiology of Heart Failure

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OPEN ACCESS

Received: Jun 19, 2024 Accepted: Jul 1, 2024 Published online: Jul 17, 2024

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Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest

Dr. Tromp is supported by the National University of Singapore Start-up grant, the tier 1 grant from the Ministry of Education and the CS-IRG New Investigator Grant from the National Medical Research Council; has received research support from AstraZeneca

AUTHOR'S SUMMARY

Heart failure (HF) characteristics, treatment, and clinical outcomes vary significantly across different world regions. The local prevalence of HF etiologies, such as ischemic and hypertensive heart disease, and region-specific health system constraints significantly impact this variation. Our review highlights the importance of considering these regional differences when designing and implementing HF management strategies and clinical trials. By aligning HF treatments and interventions with the specific needs and circumstances of populations in different geographic areas, we can enhance the effectiveness of care and improve outcomes on a global scale. If treatment strategies are adapted to be less resource-intensive and more suited to local healthcare environments, they have the potential for broader implementation and more significant impact.

ABSTRACT

Heart failure (HF) epidemiology, patient characteristics, and clinical outcomes exhibit substantial regional variations, reflecting diverse etiologies and health system capacities. This review comprehensively analyses these variations, drawing on data from recent global registries and clinical trials. Our review indicates that ischemic and hypertensive heart diseases are prevalent globally but differ in dominance depending on the region. Notably, regions such as Africa and Latin America show higher instances of HF from hypertensive heart disease and Chagas cardiomyopathy, respectively. Moreover, disparities in age and comorbidity profiles across regions highlight younger populations with HF in lower-income countries compared to older populations in high-income regions. This review also highlights the global disparity in guideline-directed medical and device therapy, underscoring significant underuse in lower-income regions. These insights emphasize the need for targeted HF management strategies considering regional clinical and demographic characteristics to enhance global HF care and outcomes.

Keywords: Geographical differences; Heart failure; Lower middle income



and consulting or speaker fees from Us2.ai, and owns patent US-10702247-B2 unrelated to the present work.

Other author has no financial conflicts of interest.

Data Sharing Statement

The data generated in this study is available from the corresponding author upon reasonable request.

Author Contributions

Writing - original draft: Tromp J, Katherine Teng TH; Writing - review & editing: Tromp J, Katherine Teng TH.

INTRODUCTION

In 2017, approximately 64.3 million people were suffering from heart failure (HF) globally.¹⁾ Its prevalence continues to increase due to the ageing demographics, population growth and treatment progress in HF which has significantly improved long-term clinical outcomes.²⁾ The age-standardized HF incidence increases in lower-income countries while decreasing in high-income countries.³⁾

Patients outside Western Europe and the United States have historically been underrepresented in HF clinical trials and registries. Yet, most patients living with HF live in non-western countries.⁴ Furthermore, HF clinical trials are increasingly globalized due to increasing sample size requirements and the recognition of possible ethnic and geographic treatment effects and regulatory requirements.⁵

Understanding regional differences in HF epidemiology, including patient characteristics, outcomes, and treatment, is a significant unmet need to inform future clinical trials and treatment quality improvement programs. Previous reviews have provided an overview of regional differences in HF.⁴⁻⁷⁾ However, the publication of important new information, including from key registries, shed additional light on regional differences in HF, not covered in previous reviews.⁸⁻¹⁰

Therefore, this narrative review summarizes the most recent data on differences in patient characteristics, clinical outcomes, and treatment in patients with HF. Information in this review can help inform global or regional quality improvement programs and the design of global clinical trials. This review classifies countries according to a modified classification of World Health Organization regions: North America, Central and South America, Western Europe, Eastern Europe, the Eastern Mediterranean, Africa, Southeast Asia, and the Western Pacific (**Figure 1**).

REGIONAL DIFFERENCES IN AETIOLOGY

Overall, ischemia and hypertensive heart disease are the most common HF aetiologies globally.¹¹⁾ There is significant between and within regional variation in HF aetiology. For example, while ischemic heart disease is the most common aetiology in high-income regions, hypertensive heart disease is more common in African American patients than those of other descent in North America.¹²⁾ In Central and South America, Chagas cardiomyopathy, a late-stage complication of Chagas disease caused by the protozoan Trypanosoma cruzi, is a common cause, especially in Brazil and Argentina.¹³⁾ In Central and Eastern Europe, alcoholic cardiomyopathy is a more common cause of HF than in other world regions, offering a unique opportunity for prevention.¹⁴⁾ Data from the International Congestive Heart Failure (INTER-CHF) study and the Soweto Heart Study, demonstrated the importance of hypertensive heart disease and human immunodeficiency virus in HF aetiology as possible causes in sub-Saharan Africa.^{15:17)} Data from Asian Sudden Cardiac Death in Heart Failure (ASIAN-HF) and International REgistry to Assess Medical Practice with lOngitudinal obseRvation for Treatment of Heart Failure (REPORT-HF) demonstrated the very high prevalence of ischemic heart disease in South and Southeast Asia,¹⁸⁻²⁰ which coincides with the increasing use of tobacco countries in many lower-income countries in this region.²¹⁾²²⁾ Valvular heart disease, especially rheumatic heart disease, is more common in Africa and Central and South America than in North America or Western Europe.²³⁾

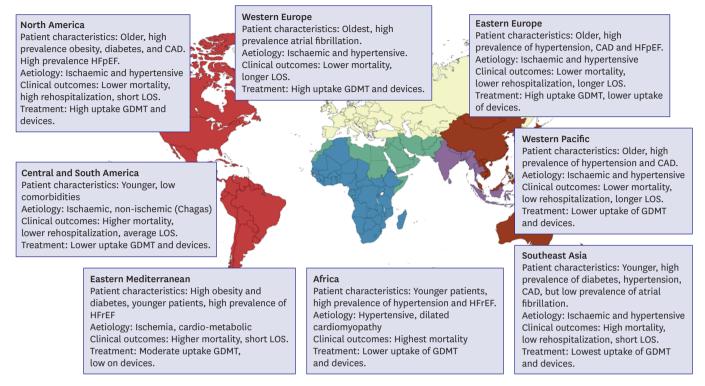


Figure 1. Regional differences in patient characteristics, aetiology, clinical outcomes and treatment around the world with heart failure. CAD = coronary artery disease; GDMT = guideline-directed medical therapy; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LOS = length of stay.

REGIONAL DIFFERENCES IN PATIENT CHARACTERISTICS

Compared to other regions, such as Central and South America or Asia, patients in North America and Western Europe are commonly older.²⁾²⁴⁾²⁵⁾ The mean age of the Get-With-the-Guidelines registry is similar to that of patients in the European Society of Cardiology (ESC) HF long-term registry,²⁶⁾ but older than patients from lower-income countries regardless of geographic region.⁹⁾ Notably North American patients in the REPORT-HF registry were younger than patients from other regions.²⁾ This difference between REPORT-HF and other registries is likely explained by the high proportion of African-American patients from urban populations enrolled in this registry.²⁷⁾ Indeed, African American patients are significantly vounger than other patients in North America. In stark contrast, patients from lower-income regions are a lot younger. For example, acute HF patients in Southeast Asia in the REPORT-HF registry were almost a decade younger than equivalent patients in Western Europe.²⁾ These differences were also seen in patients with chronic HF.9) In the Global Congestive Heart Failure (G-CHF) registry, patients from low-income countries had a median age of 59 years compared to 69 years in high-income countries.⁹⁾ These age differences were also seen in global clinical trials.²⁸⁻³³⁾ For example, patients with heart failure with preserved ejection fraction (HFpEF) from Western Europe in the PARAGON-HF trial had a mean age of 75 years compared to 71 years of patients in Eastern Europe.³³⁾ The Sub-Saharan Africa Survey of Heart Failure (THESUS-HF), a regional acute HF registry with data from 9 African countries, showed that the average of patients was only 52 years.¹⁷⁾

Global registries demonstrated that HF more commonly affects men than women.⁸⁾³⁴⁾ However, this is modified by the left ventricular ejection fraction (LVEF) phenotype, since patients with HFpEF are more commonly women than men. Notably, patients from Central and South America were more often women than men in registries.⁸⁾³⁴⁾ This pattern was also observed in clinical trials, such as Prospective Comparison of ARNI with ARB Global Outcomes in HF With Preserved Ejection Fraction (PARAGON-HF) (**Table 1**),³³⁾ and Prospective Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure (PARADIGM-HF) (**Table 2**).³⁵⁾

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			Geographica	al regions		
	Asia-Pacific	Central Europe	Latin America	North America	Western Europe	p value
No. of patients	762	1,715	370	559	1,390	
Demographics, clinical characteristics						
Age (years)	72±9	71±8	73±9	74±8	75±7	<0.001
Male sex (%)	50	48	40	53	48	<0.001
Body mass index (kg/m²)	28±5	31±5	30±5	32±5	30±5	<0.001
NYHA class I/II (%)	83	79	89	78	81	<0.001
NYHA class III/IV (%)	17	21	11	22	19	
LVEF (%)	58±8	56±8	59±9	59±7	58±8	<0.001
1edical history (%)						
Hypertension	92	98	96	97	94	<0.001
Atrial fibrillation/atrial flutter	34	31	30	29	36	<0.001
Diabetes mellitus	44	45	38	49	39	<0.001
Myocardial infarction	23	24	22	24	21	<0.001
Coronary artery disease	42	50	27	49	37	<0.001
eGFR <60 mL/min/1.73 m ²	54	59	53	37	46	<0.001
Aortality per 100 PY	NA	NA	NA	NA	NA	
HF hospitalization per 100 PY	NA	NA	NA	NA	NA	

Values are presented as mean ± standard deviation or number (%).

eGFR = estimated glomerular filtration rate; HF = heart failure; LVEF = left ventricular ejection fraction; NA = not applicable; NYHA = New York Heart Association; PARAGON-HF = Prospective Comparison of ARNI with ARB Global Outcomes in HF With Preserved Ejection Fraction; PY = person-years.

Table 2. Characteristics of patients with HF in PARADIGM-HF trial according to geographical regions

	8 8 8 1							
Asia-Pacific	Central/Eastern Europe/Russia	Latin America	North America	Western Europe	p value			
1,487	2,762	1,433	602	1,680				
57.8±12	65.1±10	63.0±12	65.1±11	68.3±10	<0.0001			
80	77	73	83	82	<0.0001			
24±4	30±5	27±5	31±7	29±5	<0.0001			
28±6	32±5	28±6	27±7	30±6	<0.0001			
87	56	89	80	81	<0.0001			
13	44	11	20	19				
58	70	43	63	58	<0.0001			
48	87	68	84	63	<0.0001			
17	52	24	40	44	<0.0001			
35	34	27	49	36	<0.0001			
27	34	35	52	45	<0.0001			
2	7	4	54	33	<0.0001			
73	83	78	81	81	<0.0001			
89	95	92	97	94	<0.0001			
56	61	65	36	44	<0.0001			
8.9	8.3	10.1	7.9	6.7	<0.0001			
12.5	12.3	11.2	13.6	9.6	<0.0001			
	57.8±12 80 24±4 28±6 87 13 58 48 17 35 27 2 73 89 56 8.9	Asia-Pacific Central/Eastern Europe/Russia 1,487 2,762 57.8±12 65.1±10 80 77 24±4 30±5 28±6 32±5 87 56 13 44 58 70 48 87 17 52 35 34 27 34 2 7 73 83 89 95 56 61 8.9 8.3	Asia-PacificCentral/Eastern Europe/RussiaLatin America1,4872,7621,43357.8±12 65.1 ± 10 63.0 ± 12 807773 24 ± 4 30 ± 5 27 ± 5 28 ± 6 32 ± 5 28 ± 6 87 56 89 13 44 115870 43 48 87 68 17 52 24 35 34 27 27 34 35 27 4 73 83 788995 92 56 61 65 8.9 8.3 10.1	$1,487$ $2,762$ $1,433$ 602 57.8 ± 12 65.1 ± 10 63.0 ± 12 65.1 ± 11 80 77 73 83 24 ± 4 30 ± 5 27 ± 5 31 ± 7 28 ± 6 32 ± 5 28 ± 6 27 ± 7 87 56 89 80 13 44 11 20 58 70 43 63 48 87 68 84 17 52 24 40 35 34 27 49 27 34 35 52 2 7 4 54 73 83 78 81 89 95 92 97 56 61 65 36 8.9 8.3 10.1 7.9	Asia-PacificCentral/Eastern Europe/RussiaLatin AmericaNorth AmericaWestern Europe1,4872,7621,433 602 1,68057.8±12 65.1 ± 10 63.0 ± 12 65.1 ± 11 68.3 ± 10 80777383 82 24±4 30 ± 5 27 ± 5 31 ± 7 29 ± 5 28±6 32 ± 5 28 ± 6 27 ± 7 30 ± 6 87568980811344112019587043 63 584887 68 84 63 17522440443534274936273435524527454337383788181899592979456616536448.98.310.17.96.7			

Values are presented as mean ± standard deviation or number (%).

CRT-D = cardiac resynchronization therapy-defibrillator device; eGFR = estimated glomerular filtration rate; HF = heart failure; ICD = implantable cardioverter defibrillator; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid receptor antagonist; NYHA = New York Heart Association; PARADIGM-HF = Prospective Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure; PY = person-years.

Multimorbidity is more common in North American and Western European patients than in other regions, which significantly complicates treatment and impedes patient prognosis.¹¹⁾ Especially cardiometabolic comorbidities, such as obesity, hypertension, and diabetes, are particularly common in patients from North America.¹¹⁾³⁶⁾ In Western Europe, patients have a higher prevalence of rhythm disorders associated with more advanced age, such as atrial fibrillation.³⁷⁾ The prevalence of comorbidities in Central and South America is lower than in most registries.⁹⁾¹⁰⁾¹⁶⁾ This might partly be explained by the high prevalence of Chagas cardiomyopathy. These patients are commonly younger and have fewer comorbidities.³⁸⁾ Data from the Gulf Acute Heart Failure Registry (Gulf CARE) showed that patients from seven Gulf countries had a higher prevalence of diabetes and heart failure with reduced ejection fraction (HFrEF), with a lower prevalence of atrial fibrillation.³⁹⁾ The ASIAN-HF registry showed that both patients with HFpEF and HFrEF in South and Southeast Asia have a higher burden of comorbidities, especially diabetes, obesity, and hypertension, despite being more than a decade younger than their Western counterparts.¹⁸⁾¹⁹⁾⁴⁰⁻⁴²⁾ Uniquely, South Asian patients with HF have a very low prevalence of AF.¹⁸⁾⁴⁰⁾ Results, which have also been confirmed in South Asian diaspora in Western Europe, suggest ethnic or genetic effects.⁴³ In the Western Pacific, Japan has among the oldest patients globally. In these patients, frailty and cognitive decline are common comorbidities, while these patients have a low prevalence of diabetes and obesity.⁴⁴⁾ In Africa, patients with acute HF were reported to have few comorbidities, except for hypertension.¹⁷⁾ In THESUS-HF, over half (55%) of patients reported a history of hypertension, despite their relative youth.¹⁷⁾ This observation is also seen in patients of black or African descent in North America.²⁷) This suggests that genetic factors might explain the high prevalence of hypertension, which has been described previously.⁴⁵⁾

REGIONAL DIFFERENCES IN CLINICAL OUTCOMES

Previous studies reporting differences in mortality showed stark differences. In REPORT-HF, post-discharge mortality was higher in lower- and middle-income countries (LMICs), especially in Southeast Asia and the Eastern Mediterranean region (Table 3).²⁾ When stratifying this data to those with HFrEF and HFpEF, the regional differences in mortality were most significant in patients with HFrEF, suggesting that treatment quality might be an important factor.⁴⁶⁾ These results were mirrored in the G-CHF registry (**Table 4**): mortality was highest in LMICs and lower in high-income regions.⁹⁾ In G-CHF, mortality was worst in Africa, followed by Asia and South America, despite patients being significantly younger in these regions.⁹⁾ The ASIAN-HF registry showed similar regional differences within Asia.⁴⁰⁾ Here, mortality was highest in Southeast and South Asia and lower in Northeast Asia, which includes Japan and South Korea.⁴⁰⁾ In the PARADIGM-HF trial, mortality was highest in Latin America and the Asia Pacific region and lowest in North America and Western Europe.³⁵⁾ Results from REPORT-HF might explain some of these regional differences.²⁾ In REPORT-HF, we found that patients from lower-income countries more often presented with new-onset HF than those in higher-income countries. Furthermore, patients with new-onset HF in LMICs in REPORT-HF often had worse signs and symptoms than those from higher-income regions.²⁾ This suggests that patients from LMICs might face barriers in seeking care, as they present later in their HF journey for specialist care, leading to treatment delays.⁴⁷⁾

A shorter length of stay (LOS) is often connected to a higher risk of readmission.⁴⁸⁾ However, rehospitalization rates are also compounded by health system considerations, including admission barriers such as out-of-pocket (OOP) costs.⁴⁹⁾ Consequently, previous studies

Table 3. Characteristics of patients with HF stratified by geographic regions in the REPORT-HF registry

	REPORT	-HF	Geographical regions								
	Overall	Missing No.	North America	Western Europe	Eastern Europe	Southeast Asia	Eastern Mediterranean & Africa	Central & South America	Western Pacific		
No. of patients	18,102		1,565	3,489	2,761	2,292	2,172	2,525	3,298		
Demographics & clinical characteris	stics										
Age (years)	67 (57–77)		63 (54-73)	75 (65-81)	68 (60-77)	61 (53-77)	64 (55-73)	67 (57-77)	67 (56-77)		
Male sex (%)	61		59	64	58	64	62	60	61		
In-patient enrollment	All inpatient enrolments										
Ischemic aetiology	6,034 (40)		336 (27)	1,101 (40)	1,148 (45)	715 (37)	864 (48)	594 (31)	1,276 (44)		
NYHA class III/IV	7,009 (38)	7,030	331 (21)	1,111 (32)	1,288 (47)	818 (32)	1,065 (49)	976 (29)	1,420 (44)		
LVEF ≥40% (%)	48	1,562	44	45	63	41	42	44	50		
Body mass index (kg/m ²)	26 (23-31)	9,396	29 (24-36)	27 (24-32)	27 (24-31)	23 (20-26)	27 (24-31)	25 (23-31)	24 (21-27)		
Systolic blood pressure (mmHg)											
Comorbidities (%)											
Hypertension	64	20	77	63	80	47	60	68	55		
Diabetes mellitus	37	6	42	37	33	42	47	31	32		
Chronic kidney disease	20	6	34	26	23	10	18	17	15		
Coronary artery disease	48	19	47	44	62	51	52	33	49		
Atrial fibrillation	31	20	38	46	47	8	21	27	25		
Treatment & device therapy (%)											
ACEI/ARB/ARNI	70	29	63	74	75	56	73	73	73		
Beta-blockers	76	29	85	89	87	50	75	83	71		
MRA	59	29	44	63	72	38	50	73	71		
Loop diuretic	86	29	89	92	92	84	90	80	78		
ICD	3,788		39	26	11	2	6	14	4		
1-year mortality (%)	20		21	20	16	21	22	23	17		
HF hospitalization within 1-year	22		41	24	24	11	23	20	20		
Length of stay (days)	8 (5-12)		6 (4-10)	9 (6-13)	9 (6-13)	6 (4-8)	6 (4-10)	8 (5-14)	9 (7-14)		

Values are presented as mean ± standard deviation, median (range), or number (%).

ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor/neprilysin inhibitor; HF = heart failure; ICD = implantable cardioverter defibrillator; LVEF = left ventricular ejection fraction; MRA = mineralocorticoids receptor antagonist; NYHA = New York Heart Association; REPORT-HF = International REgistry to Assess Medical Practice with lOngitudinal obseRvation for Treatment of Heart Failure.

Table 4. Characteristics of patients with HF stratified by geographic regions in the G-CHF registry

	G-CHF			Geographical regions						
	Overall	Missing No.	North America	Western Europe	Eastern Europe	East Asia	South Asia	Africa	South America	Middle East
No. of patients	23,291		2,710	3,826	1,814	1,894	2,974	5,352	2,897	1,824
Demographics & clinical characteri	stics									
Age (years)	65±13		65±13	71±12	66±12	66±15	59±13	57±17	67±12	58±14
Male sex (%)	61		70	68	64	59	64	46	62	68
In-patient enrolment	7,362 (32)	4	437 (16)	1,097 (29)	637 (35)	880 (47)	1,532 (52)	1,851 (35)	406 (14)	522 (29)
Ischaemic aetiology	8,871 (40)	1,208	1,164 (46)	1,523 (43)	975 (57)	909 (50)	1,427 (54)	621 (12)	1,269 (46)	983 (55)
NYHA class III/IV	9,208 (40)	117	920 (35)	1,224 (32)	565 (31)	1,116 (59)	1,276 (43)	2,685 (50)	820 (28)	602 (33)
LVEF ≥40% (%)	46	3,936	41	49	66	60	34	47	46	27
Body mass index (kg/m²)	27 (23-31)	564	29 (25-34)	28 (25-32)	30 (26-34)	24 (21-26)	24 (21-27)	24 (21-29)	28 (24-31)	29 (25-33)
Systolic blood pressure (mmHg)	118±19	64	118±19	124±19	128±16	125±19	123±20	124±26	123±21	124±22
Comorbidities (%)										
Hypertension	66	2	67	72	83	58	51	61	78	61
Diabetes mellitus	31	2	39	32	34	25	42	12	33	49
Chronic kidney disease										
Coronary artery disease	38	1	49	44	61	45	53	6	41	38
Atrial fibrillation	27	2	43	46	45	31	12	12	23	18
Treatment & device therapy (%)										
ACEI/ARB/ARNI	77	7	79	83	87	71	57	76	83	83
Beta-blockers	80	8	88	89	88	77	74	64	86	94
MRA	55	10	79	83	87	71	57	76	83	83
Loop diuretic	79	10	72	77	77	79	82	92	63	79
1-year mortality (%)	19		17	15	12	13	17	30	16	13

Values are presented as mean ± standard deviation, median (range), or number (%).

ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor/neprilysin inhibitor; G-CHF = Global Congestive Heart Failure; HF = heart failure; LVEF = left ventricular ejection fraction; MRA = mineralocorticoids receptor antagonist; NYHA = New York Heart Association. showed that HF (re)admission rates are highest in regions with a shorter LOS and lower admission barriers, such as OOP costs.²⁾ In PARADIGM-HF, the risk of HF rehospitalization was lowest in Western Europe, Latin America, and the Asia-Pacific region and highest in North America (**Table 2**).³⁵⁾

REGIONAL DIFFERENCES IN CARE-SEEKING BEHAVIOUR

Regional differences in care-seeking behaviour and care quality might explain the geographical differences in mortality and rehospitalization described in the previous section.

High OOP costs are a significant barrier to seeking care. OOP costs are especially high in Southeast Asia and Latin America, which may explain the lower hospitalization rate.⁵⁰ The fact that mortality is higher in Latin America and Southeast Asia than in other regions suggests that disease severity is not driving differences in rehospitalization rates. Indeed, in G-CHF there was a disconnect between rehospitalization rates and death such that the 30day case fatality rate was higher in LMICs than higher income countries.⁹⁾ Single-country data from LMICs, such as Tanzania and Ethiopia, suggest that structural barriers, such as distance to health facilities and high OOP, are significant factors in determining treatment delay.⁵¹⁾⁵²⁾ Financial barriers also exist in high-income countries.⁵³⁾ In a previous study from the United States using data from the Medical Expenditure Panel Survey-Household Component (MEPS-HC), patients with public insurance and patients without insurance were more likely to delay seeking care than patients with private insurance.⁵³ In an extensive multinational registry involving over 18,000 patients from 44 countries, uninsured patients were commonly vounger and had more advanced disease than patients with health insurance.⁴⁶ These examples illustrate the significant impact of financial barriers on care-seeking behaviour. Not having access to health insurance coverage early in the disease could mean risking higher morbidity and catastrophic healthcare spending later in life.

REGIONAL DIFFERENCES IN QUALITY OF CARE

This section summarizes information from several reports on regional differences in acute HF therapy, the use of guideline-directed medical therapy (GDMT), device use (**Figure 1**), and sex differences.

Acute heart failure therapies

Previous data on regional differences in acute HF therapy have predominantly come from clinical trials²⁹⁻³¹ or regional registries from the United States,⁵⁴⁾⁵⁵ Western Europe,²⁶⁾ Africa,¹⁷⁾ or the Asia-Pacific region.⁵⁶⁾ The recent REPORT-HF registry reported the first global comparison of acute HF therapies across different regions (**Table 3**).⁵⁷⁾

In the Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF) trial, patients from Eastern Europe had half the daily loop diuretic dose than those from North America.²⁹⁾ This is likely explained by the longer LOS in patients from Eastern Europe than in North America. An analysis comparing time-to-diuretics across regions showed that patients from Eastern Europe and Southeast Asia had shorter time-to-diuretics than others.⁵⁸⁾ Time to treatment was especially short in patients admitted to the intensive care unit.⁵⁷⁾ Notably, patients from Eastern Europe, the Western Pacific, and

Southeast Asia were 3 times more likely to use inotropic agents than patients from North America and Western Europe.⁵⁷⁾

Acute HF trials and registries have reported significant geographic differences in LOS.²⁹⁻³¹⁾⁵⁷⁾ In REPORT-HF, the median LOS was 6 days in North America, the Eastern Mediterranean, and Southeast Asia, and nine days in Western and Eastern Europe and the Western Pacific (**Table 3**).⁵⁷⁾ These results were mirrored in the ASCEND-HF trial.²⁹⁾ In this trial, the median LOS varied from 5 days in the Asia/Pacific and North American regions to 8 days in Western Europe and ten days in Central Europe.²⁹⁾ Similarly, in the Aliskiren Trial on Acute Heart Failure Outcomes (ASTRONAUT) study, the median LOS was 5 days in North America and the Asia/Pacific region and longest in Western (10 days) and Eastern (11 days) Europe.³¹⁾ In Africa, patients enrolled in the THESUS-HF registry had a median LOS of 7 days.¹⁷⁾

Guideline-directed medical therapy for heart failure

Use of the four pillars of GDMT, sodium-glucose cotransporter-2 inhibitors, mineralocorticoids receptor antagonists (MRAs), beta-blockers and angiotensin receptor/ neprilysin inhibitor (ARNI), by patients with HFrEF, reduces the risk of mortality and morbidity.⁴⁷) Yet, despite the significant benefits, GDMT remains underused.⁹⁾⁴⁶⁾⁵⁹⁻⁶²)

In North America, data from the Change the Management of Patients With Heart Failure (CHAMP-HF) registry showed that only 23% of patients were on ≥50% of guidelinerecommended target dosages (GRTD) for angiotensin-converting enzyme inhibitors (ACEis)/ angiotensin receptor blockers (ARBs), and only 36% for beta-blockers.⁵⁹ In Europe, the QUALIFY registry showed that 63% of patients were at ≥50% of GRTD for ACEis and 39.5% for beta-blockers.⁶²⁾ Importantly, there were significant geographical differences, with patients from Central/Eastern Europe less likely to be on GRTD.⁶² Data from the REPORT-HF registry showed that the use and dosages of GDMT were lower in lower- than higher-income regions.⁴⁶⁾ Usage of GDMT was particularly low in patients with HFrEF from Southeast Asia and the Western Pacific.⁴⁶⁾ A regional analysis from ASIAN-HF showed that guideline-recommended dose was only achieved in 17% of patients with HFrEF for ACEi, 13% for beta-blockers, and 29% for MRA.⁶¹ In this analysis, the use of GDMT was lower in Southeast Asian countries than in the Western Pacific.⁶¹⁾ These prior results were confirmed by more recent data from G-CHF, showing significantly lower use of GDMT in lower-income countries.⁹⁾ Data from INTER-CHF and THESUS-HF, suggest that GDMT is lower in African countries than in North America and Western Europe, following similar patterns observed in Southeast Asia and the Western Pacific.^{16]17)} Data from the Middle East suggest that the use of GDMT in this region is closer to that seen in Western Europe and North America.¹⁶ Factors possibly explaining these geographical differences include health system payment mechanisms and OOP costs.⁶³⁾

Cardiac devices

Cardiac devices, such as implantable cardioverter defibrillators, significantly improve survival in eligible patients.⁶⁴⁾ Despite similar indications, there are stark regional differences in device usage, which are more pronounced than regional differences in GDMT.⁶⁵⁾ In G-CHF, only 0.3% of patients from lower-income countries had an implantable cardioverter defibrillator (ICD) compared to 30.3% in higher-income countries.⁹⁾ Data from REPORT-HF showed similar results.²⁾ A sub-analysis of ASIAN-HF, showed that ICD usage varied across Asia from 1.5% in Indonesia to 52.5% in Japan. Importantly, a sub-analysis of 2,000 ICD nonrecipients showed that 55% of patients were either unaware of the benefits or needed more information on device therapy, which might explain some regional differences.⁶⁶⁾ Perhaps most importantly,

ICD devices are comparatively expensive and are less cost-effective than GDMT.⁶⁰ Lack of reimbursement for ICDs in LMICs plays a prominent role in explaining the disparity.⁶⁷

CONCLUSION

This narrative review underscores the profound regional disparities in HF characteristics, treatments, and outcomes across various global populations. These differences highlight the critical need for region-specific HF management programmes. Future efforts should prioritize inclusive and diverse clinical trials that reflect the demographic and clinical realities of HF globally. Enhancing access to HF therapy and improving healthcare infrastructures in LMICs are essential. By tailoring strategies to the unique needs of each region, we can improve HF care and outcomes worldwide, ultimately moving towards an equitable health system that addresses the diverse HF population's needs.

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